Important themes in neuro-oncology practice: Rare brain tumors, radiotherapy and its side effects, and supportive and palliative care

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Editorial

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The present issue of Neuro-Oncology Practice has a focus on rare brain tumors, radiotherapy, radionecrosis, and supportive and palliative care.

Using National Cancer Database data, Prabhu and colleagues (pXXX) assessed an association of post-operative ("adjuvant") radiotherapy with outcome in adult patients with intracranial ependymoma. No association of administering radiotherapy with survival was detected, although other factors like older age and male sex showed such an association. While these data are interesting and somewhat surprising, it remains doubtful that uncontrolled data like this will change what has become a common practice at many sites. Siddiqui and colleagues (pXXX) provide contemporary data on the risk of radiation necrosis after radiosurgery for brain metastasis. The risk per lesion at 4 years was estimated at 6.8%, and 60% of patients had an intervention for radiation necrosis. Re-irradiated lesions had a radiation necrosis risk at 4 years of 33.3%. Bevacizumab has emerged as probably the most potent medical treatment for radiation necrosis and this has now has also been confirmed in children with symptomatic radiation necrosis (Baroni et al., pXXX). Long-term survival with adequate health-related quality of life has become the major goal of clinical interventions in brain tumor patients. Data on long-term consequences of brain tumor treatment are still scarce, but cerebrovascular complications are increasingly noted. A cross-sectional study from Finland, studying pediatric brain tumor patients after a median of 20 years after radiotherapy, confirmed a high rate of 63% of cerebrovascular disease that was diagnosed at a median age of 27 years (Remes pXXX). Cerebrovascular disease, small vessel

disease or large vessel disease were noted in 52%, 38% and 16% of the patients. Six patients had experienced a stroke, 2 patients had experienced cerebral hemorrhage. The risk was increased by the classical risk factors of cerebrovascular disease like elevated blood pressure and elevated cholesterol levels. The authors stress the need for preventive strategies in this patient population, but delaying or modifying the dose of radiotherapy should also be considered in treatment-sensitive brain tumors.
Lu and colleagues (pXXX) review the efficacy and safety of bevacizumab in progressive low-grade gliomas in children and identified 7 studies reporting clinical histories of 110 patients who were treated with bevacizumab, mostly as part of combination regimens. While the rate of clinical and radiological responses was encouraging, there were no controlled data and no conclusions regarding the intrinsic activity of bevacizumab alone and an impact on survival could be derived.

An understudied aspect of cancer chemotherapy for malignant brain tumors of childhood concerns proactive enteral tube placements and feeding. Weight loss is a common problem in this patient population during treatment. The retrospective analysis by Bendelsmith and colleagues (pXXX) illustrates that proactive enteral tube feeding helps to maintain weight or to facilitate weight gain, at least over the first year of treatment and was acceptable for the children and their families.
There have recently been increased efforts in promoting participation of brain tumor patients in clinical trials and other research projects. In this regard, Mulhauser and colleagues (pXXX) explored the ability to provide informed consent to research in patients with brain metastases, with extra-CNS metastases or in healthy controls and, expectedly, found that patients with brain metastases showed lower performance in the domain of understanding. The authors conclude with many of our colleagues that the current research consent process is simply too complicated, may be even for healthy individuals.

The advances in molecular neuropathology have resulted in a rather sophisticated subclassification of primary brain tumors, including the generation of many new entities for which very little knowledge is available in the clinical domain. Papillary tumor of the pineal region is such a rare entity for which little guidance for management can be provided. A single center experience from Tübingen, Germany (pXXX) suggests that at least half of patients will develop local recurrence after surgery, suggesting that further treatment might be worth considering after incomplete resection. Whether this treatment should include only radiotherapy or other approaches needs to be studied prospectively.

The overall limited success of targeted therapy for primary brain tumor patients makes BRAF inhibition an attractive option for the few patients with tumors that exhibit mutations of BRAF. However, as

reported by Schreck and colleagues (pXXX), combined BRAF and MEK inhibition has the potential for significant toxicity, notably also since this treatment is usually thought to be required for a long time. Information on these caveats of targeted therapy are important for the neuro-oncology community.

There has recently been major interest in a potential role of cannabis and its derivatives in brain tumor patients, including claims of intrinsic antitumor properties. Rodriguez-Almaraz and colleagues (pXXX) set out to review the evidence and identified 5 of 45 initial publications for further study. They conclude that there was limited “moderate-quality evidence” supporting the use of cannabis as an adjunct to standard of care, but it appears that prospective controlled trials are essential before any recommendation for the use of such agents can be made.

Although guidelines uniformly recommend that patients with suspected primary brain tumors should undergo a neurosurgical procedure to secure a diagnosis, this is not uniformly adhered to in clinical practice. Sometimes such interventions are not thought to be feasible, at least at certain sites or in certain regions. There are thus little data on outcome in such patients treated based on imaging alone. A report from Toronto, Canada on 61 such patients showed poor outcome for these patients in the supratentorial compartment, although survival was 18 months in the brainstem group, raising the suspicion that not all these patients may have had malignant gliomas (pXXX). Whenever feasible, such patients should be referred to a center where an appropriate surgical intervention, at least by biopsy, can be offered.

Data from the Wake Forest Baptist Comprehensive Cancer Center registry were used by Bower and colleagues (pXXX) to study whether community economic factors where associated with outcome in patients with primary malignant gliomas. Patients from low income communities indeed experienced shorter median overall survival, indicating that the hypothesis of an impact of community economic factors may be true. Further studies are required to better understand the potential underlying reasons and to explore whether this observation can be extrapolated to other regions within and outside the US.

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